REMARKS

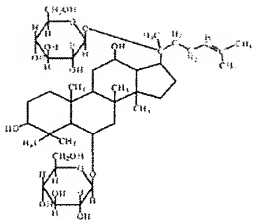
The only issue raised in the current action is whether the invention as claimed in claims 18 and 2 -12, is prima facie obvious over a combination of Gai et al Chinese Publication CN 1,273,114 and Su US Patent 4,968,675.

Gai teaches production of an injectable composition from a saponin-containing powder obtained from notoginseng by "mixing it with injection water, regulating pH value, boiling the solution adding activated carbon, filtering and fine-filtering". Su teaches production of an injectable amino-steroid drug by dissolving the active compound in a citric acid solution and then stirring in sodium citrate and sodium chloride. The product is then filtered.

The key sentence in the official action seems to be

"Although the compound taught by Su et al. is not the same as the instantly claimed compound (i.e. the compound taught by Gai et al), it is sufficiently similar as to provide valuable and relevant guidance to the skilled artisan in determining the types and amounts of buffers to use."

The examiner made a similar argument in response to the previous action. The applicant disagreed pointing out Su is concerned with salts of 16.alpha.-methyl-21-[4-[2,6-bis(1-pyrrolidinyl)-4-pyrimidinyl]-1-piperazin yl]pregna-1,4,9(11)-triene-3,20-dione In order to achieve this, Su turned to teachings relating to Ellipticine (5,11-Dimethyl-6*H*-pyrido[4,3-*b*]carbazole). These are both nitrogen-containing compounds. There is, however, no reason to think that teaching relating to either of these compounds is relevant to saponins obtained from notogiseng. Saponin RG1 referred to in the examples of the present application <u>does not contain nitrogen</u>. It has the formula:



It was therefore argued that there was no real basis for combining the teachings of Gai and Su. The examiner makes no substantive comment on these points but rather just argues that "even without the teachings of Su"the invention would be obvious. If this is the examiner's position, he should cite some alternative reference to Su to substantiate his position. Applications should not be rejected simply on the basis of unsupported assertions of the examiner. The examiner needs to explain the basis of the rejection and the factual basis for it. *In re Ahlert*, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970).

Returning now to the examiner's insistence that the compounds of Gai and Su are sufficiently similar that teaching relating to compositions containing one would be relevant to compositions containing the other, both of them are steroid derivatives, but this is the end of the similarity. They do not have the same structures; thus, persons skilled in the art would not have been motivated to apply the buffer and isotonic solution as taught in Su et al into the product of Gai et al. (i.e., Xuesaitong injection).

Steroid derivatives are general name of a variety of derivatives which are broadly distributed in nature and cover numerous substances, and it is well known that substances covered by the term "steroid derivatives" may be substantially different one another in terms of structure and physico-chemical property. For instance, ellipticine differs remarkably from the major active

ingredients of saponins obtained from Panax notoginseng (e.g., Rg1, RbI, Rl and the like) in structures, physico-chemical properties, and physiological activities, and thus they are not compounds having similar properties. In this situation, persons skilled in the art cannot conclude reasonably that a buffer suitable for ellipticine is also suitable for saponins obtained from Panax notoginseng. Thus, referring to Su et al as proposed by the examiner is not reasonable and persons skilled in the art have not been motivated to combine Gai et al with Su et al.

As for the boiling and pasteurization at 110°C step of the present application, the applicant submits respectfully that the boiling step of the claimed method is conducted prior to the addition of Panax notoginseng saponin family powders, and thus it would not affect the stability of Panax notoginseng saponins. Moreover, the step of pasteurization at 110°C is conducted after the injection is put in the fluid infusion bottle and capped. That is to say, the pasteurization step is conducted in a sealed contained, and thus would not cause any undesired reaction affecting the content of saponins, such as, oxidation. However, the boiling step of Gai et al is conducted in an open container for a period of up to 15-20 minutes. During this period, it is certain that the solvent is substantially evaporated and some undesired reactions (e.g., oxidation of saponins) are likely to occur in the system because of high temperature and exposure to air such that the content of active ingredients of the injection is reduced. It can be seen that the present application avoids the potential loss of active ingredients and uncertain change of pH.

The examiner further contends that Gai et al has taught the adjustment of pH and thus persons skilled in the art can also understand to adjust the pH of Panax notoginseng saponin injection by using a buffer because the use of buffer in injection and the optimization of pH are conventional in the pharmaceutical field. However, the applicant submits respectfully that it is not obvious to select the specific buffer and the specific pH value as taught in the present application and such selection

provides unexpected advantages of the claimed product compared to that of Gai et al, namely, the higher pH stability and thereby the higher stability of the active ingredients of the injections.

It is therefore submitted that no *prima facie* case of obviousness has been made out.

Even had such a case been made out, however, the invention as claimed would still comply with the requirements of 35 USC 103. The compositions of the present invention possess a surprising stability nowhere foreshadowed by the prior art.

In order for the examiner better to understand the improvement secured by the present invention, test results are submitted herewith which showing that the pH value of Xueshuantong injection (i.e., the product of Gai et al) declines remarkably over time while the pH value of the claimed injection show hardly decline. This is a surprising and significant difference.

It can be seen from the above that the amended claims are not obvious over the cited references, and meets the requirements of 35 USC 103.

It is therefore submitted that this application is in order for allowance and an early action to this end is respectfully solicited.

Respectfully submitted,

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